

176. (Amended) The method of claim 157 wherein the layer comprises a lawn structure.
177. (Amended) The method of claim 157 wherein the layer is a monolayer.
182. (Amended) The method of claim 157 wherein the layer is a permeation layer.
195. (Amended) The method of claim 157 wherein the sequence of the structures of the array is determined by selective activation of electrodes adjacent a common solution.
198. (Amended) The method of claim 157 wherein the electric field causes increased local concentration of reagents at the sites where the synthesis is to occur.
199. (Amended) The method of claim 157 wherein the solution contains a sodium phosphate buffer.

#### REMARKS

Applicants wish to thank the Examiner for the courtesy of the in-person interview on August 27, 2001 with Dr. Sosnowski and the undersigned. In addition to the summary made on the PTOL-413, Applicants wish to note that the following references were specifically discussed: Southern USP 5,667,667, Hollis USP 5,653,939 and Fodor USP 5,445,934. Applicant disclosed the pendency of the litigation styled *Nanogen, Inc. v. Donald D. Montgomery and Combimatrix, Corp.*, and indicated that the '302 patent was involved in that litigation. A supplemental Information Disclosure Statement and Form SB/08A are enclosed. These materials further list all references cited in the Montgomery patents.

Applicants have amended the specification to insert the sequence information as required. In addition we are filing herewith a Statement Under 37 CFR §1.821(e) regarding the filing of the sequence in a parent case. Additionally, a number of amendments are made to the specification which had been requested by the Examiner in parent cases.

Applicants have reviewed the pending claims in detail in order to correct certain dependencies, to conform the claims more specifically to specification support and to eliminate issues in providing claims corresponding to Applicant's proposed counts. Claims 205-213 have been deleted as being directed to patentably distinct subject matter from the remaining claims. Applicant intends to pursue these claims in a continuation case. Finally, with the cancellation of claims, Dr. Sosnowski and Dr. Evans should be removed as named inventors on this application. A petition for their removal is being filed herewith. In addition, a new Declaration for inventors Heller and Tu will be submitted shortly.

On August 28, 2001, the day after the interview with the Examiner, U.S. Patent No. 6,280,595 issued. The '595 patent is styled as a continuation of the application which issued as the '302 patent. Applicant has designated certain claims from the '595 patent as corresponding to the proposed counts.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,

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Dated: September 21, 2001

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**"Version with markings to show changes made"**

**In the Specification:**

The following amendments have been made to the specification:

At page 10, line 25, delete "claimed".

At page 10, line 29, delete "claimed".

At page 12, line 17, delete "claimed" and insert therefor --disclosed--.

At page 12, line 23, delete "claimed" and insert therefor --disclosed--.

At page 19, line 15, delete "which was actually fabricated, addressed with oligonucleotides, and tested".

At page 19, line 25, delete "Figure 7 shows" and insert therefor --Fig. 7a and Fig. 7b show--.

At page 19, line 27, after "micro-location" insert --, Fig. 7a showing the addressable microlocations in a neutral condition and Fig. 7b showing the addressable microlocations in a charged state--.

At page 19, line 28, delete "Figure 8 shows" and insert therefor --Figs. 8a, 8b, 8c and 8d show--.

At page 19, line 30, after "SSO-C)" insert --, Fig. 8a showing a first microlocation (ML-1) being addressed, Fig. 8b showing a second microlocation (ML-2) being addressed, Figure 8c showing a third microlocation (ML-3) being addressed and Figure 8d showing the three microlocations after being addressed and assembled--.

At page 19, line 31, delete "Figure 9 shows" and insert therefor --Figs. 9a, 9b and 9c show--.

At page 20, line 2, after "capture sequences" insert --, Fig. 9a showing specific capture sequences on addressable microlocations, Fig. 9b showing specific and nonspecific DNA adjacent

the structure of Fig. 9a, and Fig. 9c showing hybridized material adjacent microlocations ML-1 and ML-3--.

At page 20, line 3, delete "Figure 10 shows" and insert therefor --Figs. 10a and 10b show--.

At page 20, line 4, after "hybridization process" insert --, Fig. 10a showing materials adjacent microlocation ML-3 and Fig. 10b showing materials adjacent microlocations ML-3 and ML-5--.

At page 20, line 5, delete "Figure 11 shows" and insert therefor --Figs. 11a, 11b and 11c show--.

At page 20, line 7, after "mutations" insert --, Fig. 11a showing uncharged addressable microlocations, Fig. 11b showing negatively charged microlocations and Fig. 11c showing negatively charged microlocations with material denatured from microlocation ML-3--.

At page 20, line 8, delete "Figure 12 shows" and insert therefor --Figs. 12a, 12b, 12c and 12d show--.

At page 20, line 11, after "process" insert --, Fig. 12a showing uncharged microlocations, Fig. 12b showing negatively charged microlocations, Fig. 12c showing uncharged microlocations with dye and Fig. 12d showing positively charged microlocations--.

At page 20, line 12, delete "Figure 13 shows" and insert therefor --Figs. 13a, 13b and 13c show--.

At page 20, line 13, after "device" insert --, Fig. 13a showing negatively charged addressable microlocations, Fig. 13b showing two opposed substrates, one substrate being that of Fig. 13a and the other being a sister device containing an attachment layer, and Fig. 13c showing two substrates, each of which has sequences bound to the microlocations--.

At page 20, line 14, delete "Figure 14 shows" and insert therefor --Figs. 14a, 14b, 14c, 14d, 14e, and 14f show--.

At page 20, line 15, after "oligonucleotides" insert --, Fig. 14a showing addressable microlocations with blocking groups, Fig. 14b showing addressable microlocations with blocking groups in combination with a deblocking group, Fig. 14c showing blocked and deblocked addressable microlocations in the presence of monomer C, Fig. 14d showing addressable microlocations in combination with a deblocking group, Fig. 14e showing deblocked sites on microlocation ML-2 in the presence of monomer A and Fig. 14f showing microlocations with blocking groups on the terminal ends of sequences--.

At page 39, line 15, delete "Figure 7" and insert therefor --Figs. 7a and 7b--.

At page 39, line 21, delete "Figure 8" and insert therefor --Figs. 8a through 8d

At page 42, line 1, delete "claimed".

At page 42, line 18, delete "claimed" and insert therefor --disclosed--.

At page 43, line 12, delete "Figure 8" and insert therefor --Figs. 8a through 8d--.

At page 44, line 27, delete "Figure 9" and insert therefor --Figs. 9a through 9c--.

At page 45, line 24, delete "Figure 10" and insert therefor --Figs. 10a and 10b--.

At page 46, line 4, delete "claimed" and insert therefor --disclosed--.

At page 46, line 8, delete "Figure 11" and insert therefor --Figs. 11a through 11c--.

At page 49, line 1, delete "Figure 12" and insert therefor --Figs. 12a through 12d--.

At page 51, line 7, delete "Figure 13" and insert therefor --Figs. 13a through 13c--.

At page 54, line 12, delete "Figure 14" and insert therefor --Figs. 14a through 14f--.

At page 60, line 7, after "TCU" insert --(Sequence No. 1)--.

At page 60, line 8, after "AAU" insert --(Sequence No. 2)--.

At page 60, line 9, after "CTG U" insert --(Sequence No. 3)--.

At page 60, line 10, after "GU" insert --(Sequence No. 4)--.

At page 60, line 11, after "CU" insert --(Sequence No. 5)--.

At page 60, line 12, after "AGU" insert --(Sequence No. 6)--.

At page 60, line 13, after "GU" insert --(Sequence No. 7)--.

At page 60, line 14, after "ACU" insert --(Sequence No. 8)--.

At page 60, line 15, after "GAC U" insert --(Sequence No. 9)--.

At page 60, line 16, after "TU" insert --(Sequence No. 10)--.

At page 60, line 17, after "CU" insert --(Sequence No. 11)--.

At page 60, line 18, after "TU" insert --(Sequence No. 12)--.

At page 61, line 2, after "AT" insert --(Sequence No. 13)--.

At page 61, line 3, after "AGG" insert --(Sequence No. 14)--.

At page 61, line 4, after "CTC" insert --(Sequence No. 15)--.

At page 61, line 5, after "TTT T" insert --(Sequence No. 16)--.

At page 61, line 7, after "TAG" insert --(Sequence No. 17)--.

At page 61, line 8, after "ACT C" insert --(Sequence No. 18)--.

At page 61, line 9, after "TAC G" insert --(Sequence No. 19)--.

At page 61, line 10, after "AC" insert --(Sequence No. 20)--.

At page 61, line 11, after "CAT C" insert --(Sequence No. 21)--.

At page 61, line 12, after "AG" insert --(Sequence No. 22)--.

At page 61, line 13, after "GAA" insert --(Sequence No. 23)--.

At page 61, line 14, after "GGA A" insert --(Sequence No. 24)--.

At page 61, line 15, after "AAC A" insert --(Sequence No. 25)--.

At page 61, line 16, after "GAT G" insert --(Sequence No. 26)--.

At page 70, line 8, delete "the".

At page 71, line 10, delete "silica" and insert therefor --silicon--.

At page 71, line 28, delete ". Then" and insert therefor --, and then--.

At page 75, line 33, after "micro-location" insert --(Sequence No. 27)--.

At page 76, line 2, after "micro-location" insert --(Sequence No. 28)--.

At page 76, line 5, after "(TR)" insert --(Sequence No. 29)--.

At page 76, line 6, after "(TR)" insert --(Sequence No. 30)--.

At page 76, line 7, after "(TR)" insert --(Sequence No. 31)--.

At page 78, line 12, after "GAU" insert --(Sequence No. 32)--.

At page 78, line 14, after "GA" insert --(Sequence No. 33)--.

At page 78, line 15, after "CCA C" insert --(Sequence No. 34)--.

At page 78, line 16, after "CCA C" insert --(Sequence No. 35)--.

At page 78, line 17, after "CCA C" insert --(Sequence No. 36)--.

At page 78, line 18, after "CCG C" insert --(Sequence No. 37)--.

At page 78, line 19, after "ACG C" insert --(Sequence No. 38)--.

At page 89, line 4, after "CAG U" insert --(Sequence No. 39)--.

At page 89, line 5, after "GTG U" insert --(Sequence No. 40)--.

At page 89, line 7, after "ACC G" insert --(Sequence No. 41)--.

At page 89, line 9, after "AAT C" insert --(Sequence No. 42)--.

At page 89, line 10, after "TGC" insert --(Sequence No. 43)--.

At page 89, line 11, after "CAT" insert --(Sequence No. 44)--.

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**In the Claims:**

Claims 110, 116, 137, 138, 144, 145, 158, 171, 172, 173, 183, 197, 200, 201, 205-213 have been cancelled.

The claims have been amended as follows:

95. (Amended) A method for electronic synthesis of an array of separately formed ~~a plurality~~ of complex structures on a substrate, comprising the steps of:

providing a substrate having ~~a plurality~~ an array of controllable electrodes supported by the substrate,

providing first structures coupled to the electrodes, the structures having a blocked functional group,

providing a solution in contact with the array of electrodes,

applying a potential to selected electrodes where synthesis is to occur in order to cause deblocking of the first structure,

reacting a second structure with the deblocked first structure, and

repeating the steps of deblocking and reacting another structure to form the plurality of complex structures.

98. (Amended) The method of claim 95 97 wherein the polymer is a synthetic polymer.

99. (Amended) The method of claim 95 97 wherein the polymer is a biopolymer.

106. (Amended) The method of claim 95 wherein the first structure is a chemically reactive moiety ~~moieity~~.

108. (Amended) The method of claim 95 wherein the synthesis of the ~~plurality~~ of complex structures occurs without mechanical movement of electrodes.



132. (Amended) The method of claim 95 131 wherein the sequence of the complex structures in of the array is determined by selective activation of electrodes adjacent a common solution.

135. (Amended) The method of claim 95 wherein the electric field causes increased local concentration of reagents at the sites where the ~~sub-unit~~ synthesis is to occur ~~be coupled~~.

136. (Amended) The method of claim 95 wherein the solution contains a sodium phosphate buffer.

143. (Amended) A method according to claim 142, wherein said buffering solution is selected from the group consisting of: tris borate buffers, sodium chloride, sodium citrate buffers, and sodium phosphate buffers.

149. (Amended) A method according to claim 142, wherein said substrate is formed from at least one material selected from silicon, semiconductors, glass, ceramics, silicon dioxide and plastic polymers.

150. (Amended) A method according to claim 142, wherein said array of electrodes comprises at least ~~100~~ 64 electrodes.

157. (Amended) A method for electronically controlled synthesis of a plurality of complex structures on a substrate, comprising the steps of:

providing a substrate having a plurality of controllable electrodes supported by the substrate and covered with a permeable ~~non-insulating~~ layer,

providing first structures coupled to the layer ~~electrodes~~, the structures having a protected functional group,

providing a solution in contact with the array of electrodes supported by the substrate,

applying a potential to selected electrodes where synthesis is to occur,  
reacting a second structure with the first structure, and  
repeating the step of applying a potential and reacting a subsequent structure  
to form the complex structures, the synthesis of the array of structures occurring  
without mechanical movement.

161. (Amended) The method of claim ~~157~~ 160 wherein the polymer is a synthetic polymer.

162. (Amended) The method of claim ~~157~~ 160 wherein the polymer is a biopolymer.

169. (Amended) The method of claim 157 wherein the first structure is a chemically reactive  
moiety ~~moety~~.

173. (Amended) The method of claim ~~172~~ 157 wherein the layer couples the first structure  
to the electrode.

174. (Amended) The method of claim ~~172~~ 157 wherein the layer comprises a mesh structure.

175. (Amended) The method of claim ~~172~~ 157 wherein the layer comprises a porous  
structure.

176. (Amended) The method of claim ~~172~~ 157 wherein the layer comprises a lawn structure.

177. (Amended) The method of claim ~~172~~ 157 wherein the layer is a monolayer.

182. (Amended) The method of claim ~~172~~ 157 wherein the layer is a permeation layer.

195. (Amended) The method of claim 157 wherein the sequence of the structures of the  
array ~~is~~ are determined by selective activation of electrodes adjacent a common solution.

198. (Amended) The method of claim 157 wherein the electric field causes increased local  
concentration of reagents at the sites where the ~~sub-unit~~ synthesis is to ~~occur~~ be coupled.

199. (Amended) The method of claim 157 wherein the solution contains a sodium phosphate  
buffer.